REMARKS

Claims 2, 13 and 14 have been canceled.

Claim 1 has been amended by limiting R3, R4, R5 and q.

Claim 1 has also been amended by deleting R^{viii} and R^{ix}.

Claim 1 has also been amended by inserting "R6" immediately after the line identifying the substituents for R^{viii} (i.e. "R^{viii} = O, C1-7-alkyl"). Support for the addition can be found in the Specification on page 4, line 21. The substituent "R6" was then deleted from the claim.

Claim 1 has been amended by correcting a typographical error.

Claim 3 has been amended by deleting those moieties containing N.

No new matter has been added.

Rejections Under 35 USC § 112, second paragraph

The Examiner has rejected claims 1-14 as indefinite as there is no definition provided for the R6 variable.

Applicants have amended claim 1 to indicate that R6 is H, C1-7-alkyl, Ar-C1-7-alkyl, C1-3-alkyl-SO2-R^{ix}, C1-3-alkyl-C(O)-NHR^{ix} or CH_2XAr, thereby overcoming the rejection.

Rejections Under 35 USC § 103

The Examiner has rejected claims 1-14 as obvious over Gribble et al. (WO 98/50533). The Examiner contends that Gribble et al. teach compounds that inhibit cysteine and differ from the compounds of the instant invention by having hydrogen (H) at the α-carbon position on the ketone bearing ring structure as opposed to various substituents (i.e. methyl). The Examiner further contends that substituting methyl for H usually does not result in a significant difference in biological activities and concludes that it would have been obvious to replace H with methyl. Applicants respectfully traverse.

As discussed in the accompanying Declaration by Dr. Urszula Grabowska, Gribble and co-authors have published extensively in the academic literature that the compounds described in Gribble et al. are epimerically unstable and unsuitable for drug development. Dr. Grabowska discusses two such publications: Marquis et al. (2001) and Fenwick et al. (2001).

Dr. Grabowska also presents data that compares the behavior of representative compounds of the instant application and of the Gribble reference cited by the Examiner in standardized stability assessments carried out at pH 7 for periods in excess of four weeks. Here, it is evident that the compounds of the invention have a dynamic equilibrium that strongly favors one epimer. This data shows that the compounds of the instant invention provide

much greater quantities of the active principle per unit dose, which in turn means that treatment efficacy is improved and any toxicity associated with the "wrong" enantiomer is reduced. Again, as Dr. Grabowska states, this is particularly important in the prolonged or life-long treatment of the types of bone disorders in which cathepsin K is implicated such as osteoporosis.

To summarize, the compounds of the instant invention do, indeed, show a surprisingly improved result compared to those of Gribble et al. Consequently, Applicants respectfully request reconsideration and removal of the rejection.

In view of the above, Applicants submit that the claims currently pending present novel, unobvious, patentable subject matter and earnestly solicit an early and favorable response.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a three (3) month extension of time for filing a reply in connection with the present application. The Commissioner is hereby authorized to charge the fee of $1,020 to Deposit Account No. 02-2448.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Susan W. Gorman (Reg. No. 47,604) at the telephone number of the undersigned below, to conduct an

interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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